REMARKS

Status

Claims 1-54 were pending. Claims 1-30 have been withdrawn from consideration Claims 2-9 and 20-23 are cancelled in this amendment without prejudice to prosecution in this application, future applications, or copending applications. Claims 31, 32, 45, 47, 48, and 49 are amended in this amendment, and new claims 55-66 are added. Accordingly, upon entry of this amendment, claims 31-56 will be under examination. The new claims and claim amendments are not believed to add new matter.

The amendments to claims 31 and 47 find support in the specification at, e.g., paragraph [0058]. New claim 55 finds support in the specification at, e.g., paragraph [0067]. New claims 56 and 63 find support in the specification at, e.g., paragraph [0061] and Figure 4A. New claim 57 finds support in the specification at, e.g., paragraph [0107]. New claim 58 finds support in the specification at, e.g., paragraph [0146].

Claims 31-46 and 55-63 relate to an apparatus for containing multiple multivolume substrates. Claims 47-54 and 64-66 relate to a kit containing the apparatus and at least one component of a reaction to be carried out in the apparatus.

Rejections Citing 35 U.S.C. 112, Second Paragraph

Claims 45 and 49, which were rejected under 35 U.S.C. 112, second paragraph, have been amended to provide proper antecedent basis for the phrase "the component." Applicants thank the Examiner for suggesting appropriate amendments.

Rejections Reciting 35 U.S.C. 103(a)

de Macario and Garyantes

Claims 31-36 and 43-54 were rejected as allegedly obvious in view of U.S. Pat. No. 4,682,890 ("de Macario") and U.S. Pat. No. 6,565,813 or WO 99/39829 (both "Garyantes").

de Macario described an apparatus for use in horizontal beam spectrophotometers. The apparatus can include a "plate" having circular holes that can retain a drop or drops of samples to be analyzed using the spectrophotometer.

Garyantes described microtiter-like plates containing "virtual wells." According to Garyantes, "virtual wells could be any surface modification such as protrusions or slight indentations . . . as well as chemical modifications, binding sites, or other discontinuities present in slight indentations, on the plate surface . . . ." (See column 3, lines 13-22). Garyantes also indicates that this device can be made by wet etching of glass or silicon, EDM machining of metal, particularly corrosion resistant steels, other alloys such as Monel and Zircalloy, or noble metals such as gold, platinum or titanium, dry etching of glass, silicon, or other crystalline material, laser milling of any of the above materials, or molding of plastics. See column 26, lines 41-49.

The Office takes the position that one of skill reading the cited references would have found motivation to modify the de Macario "plate" so that it has a substrate made from titanium. Applicants respectfully disagree. As noted by the Office (third full paragraph on page 4 of the Office Action), the only materials specifically referred to by de Macario are glass, plastic or quartz, which are materials selected for their transparency (see column 7, lines 29-32). Nothing in the Garyantes reference would have led the skilled practitioner to substitute titanium in the de Macario plate. The Garyantes apparatus is wholly different from the de Macario plate (among many other differences, the Garyantes apparatus does not contain sample chambers that extend through a substrate). Accordingly, one of skill would have had no reason to believe materials suitable for the Garyantes apparatus (which are apparently materials selected as amenable to wet etching, EDM machining, dry etching, laser milling or molding) would be suitable for the de Macario plate (which, insofar as they were identified, are materials selected for transparency). Further, Garyantes did not suggest any advantage to titanium, but merely included it in a laundry list of diverse materials with different properties. The rationale relied on by the Office, that use of titanium would be "advantageous over glass, plastic or quartz since it would not be as fragile as a glass, plastic or quartz substrate," is not found in either Garyantes or de Macario, but is invented by the Office. There is no suggestion in any reference that materials (*i.e.*, glass, plastic or quartz) specifically identified by de Macario as useful in the de Macario device were undesirably fragile. Rather, these materials were specifically identified as suitable by the de Macario inventors.

To establish *prima facie* obviousness, the Office must show that one of ordinary skill would have had motivation to combine the teachings of references relied on, and that if combined

the references would have provided reason or motivation for one of skill to make the claimed apparatus. In the present application, one of skill would have had no motivation to combine the teachings of the two references relied on by the Office, because they describe wholly unrelated devices (notwithstanding the observation that both devices can be used to hold liquid samples, they are structurally and functionally dissimilar).

Further, even if combined, there would have been no motivation to make the substitution proposed by the Office: Nothing in Garyantes suggested it would have been advantageous to use titanium in de Macario's device. Instead, if the references were combined as suggested by the Office, it would be most plausible to conclude that the de Macario plate should be made from glass or plastic, since those are the materials identified in both references as useful. Indeed, the only motivation for modifying the de Macario device in the manner suggested by the Office comes from Applicants' own disclosure. It is well established that obviousness cannot be established by using an applicant's teachings as a blueprint for selecting elements from the prior art. Applicants respectfully request this rejection be withdrawn.

In addition to the arguments presented above, several of the pending claims warrant specific comment:

Claims 45 and 59, and corresponding dependent claims, are directed to an apparatus comprising at least one component of a reaction to be carried out in the apparatus, where the component is a reagent used in a nucleotide sequencing reaction, a hybridization reaction, or a polynucleotide amplification reaction. Claims 64-66 are directed to a kit containing such an apparatus. The Office acknowledges that the Garyantes or de Macario references are silent as to performing nucleic acid reactions. Commenting on this silence, the Office asserts that "nucleic acid reactions or assays are notoriously well known in the art a[s] biochemical or biological reactions. As a result, it would have been obvious to one of ordinary skill in the art to employ the device of deMacario et al. to perform any know[n] nucleic acid assay . . ." Applicants respectfully disagree. Nucleic acid reactions such as a nucleotide sequencing reaction, a hybridization reaction, or a polynucleotide amplification reaction take place at elevated temperatures (in some cases approaching 100°C). Nothing in de Macario suggested carrying out any "biochemical assay" that requires an elevated temperature, and Applicant's submit that even a cursory review of the drawing

in the de Macario reference make it plain that the de Macario apparatus is not suited for such reactions. Accordingly, nothing in the cited references suggested the claimed invention, and this rejection should be withdrawn.

Claims 50, 51, 52 and 66 recite a kit containing an apparatus of the invention and a hydrophobic substance, which can be a hydrophobic medium[1] or cover. The Office does not explain how the claimed combination is suggested by the cited references, but merely asserts it would have been "obvious" to one of skill to include "all of the components" required to . . . . [*etc.*]" Applicants respectfully submit that such merely conclusory language is not sufficient to establish any case of *prima facie* obviousness. Further, Applicants respectfully submit that the conclusion set forth by the Office is clearly incorrect. First, nothing in the cited references suggested either a cover or a need for such a cover. For example (and not for limitation), one use of the cover of the present invention is to prevent evaporation for reactions conducted at elevated temperature. As explained above, the references relied on by the Office do not describe such reactions. Further, the use of a cover is *inconsistent* with the teaching of de Macario. The de Macario apparatus is a spectrophotometric device in which it is desirable to *minimize* the number of layers of material through which an analyzing light beam must pass (see, e.g., de Macario column 7). Nothing in de Macario suggested that additional layers of materials in the form of covers were contemplated, nor would one of skill have been motivated to provide the de Macario plate in combination with a hydrophobic cover.

New claim 55 is directed to an apparatus in which the top and bottom surfaces contain raised features which form closed curves circumscribing the openings to the sample chambers. Nothing in Garyantes or de Macario, individually or in combination, suggested an apparatus with this feature.

New claim 56 is directed to an apparatus with chambers that have a hydrophobic annular ring on the wall of the chamber, separating two hydrophilic regions. Nothing in Garyantes or de Macario, individually or in combination, suggested an apparatus with this feature.

[1] It appears the Office believes the hydrophobic fluid is used to coat the substrate. However, the fluid referred to is actually used to reduce evaporation, as described in the specification at, *inter alia*, paragraphs [0083] - [0084].

Hunter and Garyantes

Claims 31, 33-42, 46, 47, 50-54 were rejected as allegedly obvious in view of WO 99/34920 ("Hunter") and U.S. Pat. No. 6,565,813 or WO 99/39829 (both "Garyantes").

Hunter described an apparatus, consisting of a platen having a plurality of through-holes. Hunter teaches that the apparatus meets "a need . . . for new approaches that permit analysis of a million samples in a laboratory format" by providing substrates with through-holes at a very high density in excess of 10^8 per square meter (see Hunter at page 1, lines 21-27 and page 2, line 16). Consistent with Hunter's requirement for very high density, Hunter teaches that through-holes are long and narrow. For example, see, page 6, lines 15-22 (teaching 100-400 μm through-holes in a 1-2 mm thick substrate) and page 6 line 27 to page 7, line 11 (teaching 100 μm through-holes in a 1.2 mm thick substrate). Hunter described chimney-like height-diameter aspect ratios of about 6:1, quite different from the chambers of the apparatus of the present invention which have an aspect ratio less than or equal to 2:1. Hunter not only *does not describe* an apparatus with chambers having an aspect ratio less than or equal to 2:1, the chambers of the present invention are *inconsistent* with and *incompatible* with Hunter's teachings. For example, chambers with a height to diameter ratio of 2:1 or less in the 1 mm thick platen of Hunter would be at least 0.5 mm in diameter. While the maximum number of 0.5 mm diameter chambers can be calculated as 20 per linear centimeter, or 400 per square centimeter, that number would be impossible to achieve because that density assumes that the spacing between holes is zero. A more accurate *maximum* density of such chambers, based on Hunter's that the center-to-center distance between through-holes are preferably about twice the diameter (see Hunter at page 6, lines 18-19), is about 100 per square centimeter. This is more than two orders of magnitude lower than the density taught by Hunter ("in excess of 10^8 per square meter") and inconsistent with the explicit teachings of the Hunter reference. Even arraying the chambers in a hexagonal pattern to increase density (by a factor of about 1.2) would result in a hypothetical density far below that required by Hunter. In summary, Hunter *teaches away* from modifying his apparatus to have the properties of the presently claimed invention.

Garyantes is described above. Garyantes described microtiter-like plates containing "virtual wells," which could be a "surface modification such as protrusions or slight indentations . . . as well

as chemical modifications, binding sites, or other discontinuities present in slight indentations, on the plate surface . . . ." (See column 3, lines 13-22).

The Garyantes apparatus is wholly different from the Hunter platen. Among many other differences, the Garyantes apparatus does not contain sample chambers that extend through a substrate. Accordingly, one of ordinary skill in the art would not have found motivation in Garyantes to modify the Hunter platen.

Further, even if the Hunter platen was modified in the manner suggested by the Office, the resulting device would be quite different from the presently claimed invention. The chamber configuration of the Hunter device is quite different from that of the present invention and, as discussed above, Hunter *teaches away* from modifying the chamber dimensions.

In addition to the arguments presented above, several of the pending claims warrant specific comment:

Claims 52 and 66 recite a kit containing an apparatus of the invention and a hydrophobic cover. The comments by the Office in articulating this rejection parallel the rejection of the same claims as allegedly obvious in view of de Macario and Garyantes, as does Applicants' response: The Office does not argue that the claimed combination is suggested by the cited references, but merely asserts it would have been "obvious" to one of skill to include "all of the components" required to . . . . *etc.*" Applicants respectfully submit that such merely conclusory language is not sufficient to establish any case of *prima facie* obviousness. Further, Applicants respectfully submit that the conclusion set forth by the Office is clearly incorrect. First, nothing in the cited references suggests either a cover or a need for such a cover. For example (and not for limitation), one use of the cover of the present invention is to prevent evaporation for reactions conducted at elevated temperature. As explained above, the references relied on by the Office do not describe such reactions.

New claim 55 is directed to an apparatus in which the top and bottom surfaces contain raised features which form closed curves circumscribing the openings to the sample chambers. Nothing in Garyantes or Hunter, taken individually or in combination, suggested an apparatus with this feature. Such raised features would be incompatible with the device described by the Hunter

reference, because Hunter teaches that flanges should be on one surface only (the other surface having indentations for stacking) rather than on both surfaces (see, e.g., page 6, lines 8-11).

New claim 56 is directed to an apparatus with chambers that have a hydrophobic annular ring on the wall of the chamber, separating two hydrophilic regions. Nothing in Garyantes or Hunter, taken individually or in combination, suggested an apparatus with this feature. Such a configuration is useful, for example and not limitation, for hot-start PCR (see, e.g., page 21, lines 17-24 of the specification).

Alleged Double Patenting Rejections

The Office has provisionally rejected claims 31-54 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims of copending Application No. 09/789,601 taken alone or in combination with Garyantes. These are provisional rejections. Applicants will respond should these rejections be made nonprovisional.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 286002023020. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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